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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,905	07/25/2003	Guido Franzoso	21459-94575	2235

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EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,905	FRANZOSO ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-37* is/are pending in the application.

4a) Of the above claim(s) *3-5,7-35 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/15/07 has been entered.

Claims 1 and 3-37 are pending.

Claims 3-5, 7-35, and 37 are withdrawn.

Claims 1, 6, and 36 have been amended by Applicant.

Claims 1, 6, and 36 are currently under examination.

Rejections Withdrawn

The rejection of claim 1 under 35 U.S.C. 112 second paragraph, for reciting "interacts", is withdrawn.

The rejection of claim 36 under 35 U.S.C. 112 second paragraph, for reciting "the peptide", is withdrawn.

The rejection of claim 36 under 35 U.S.C. 112 second paragraph, because it is not clear if a peptide that comprises the entire length of amino acids 132-156 is intended, is withdrawn.

The rejection of claim 36 under 35 U.S.C. 112 first paragraph, for failing to comply with the written description requirement, is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and dependent claims 6 and 36 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for the reasons stated in the Office Actions of 11/29/06 and for the reasons set-forth below.

Claim 1 and dependent claims 6 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Claim 1 recites "...using the agent to increase programmed cell death". However, claim 1 does not point-out the essential method step of how said agent is to be used to increase cell death. See MPEP § 2172.01. The omitted steps are: methods of *how* one is to use the agent to increase programmed cell

death. One of skill in the art would not be apprised of the metes and bounds of the claim.

The rejection was not addressed in the Reply of 8/15/07.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1 and 6 under 35 U.S.C. 112 first paragraph, as failing to comply with the written description requirement, is maintained for the reasons stated in the Office Actions of 3/30/06, 11/29/06, and for the reasons set-forth below.

The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of methods requiring use of a genus of agents that block suppression of JNK activation by Gadd45β. However, the written description in this case only sets forth HIV-TAT-Peptide 1 fusion as an example of an agent that blocks suppression of JNK activation by Gadd45β. The specification does not disclose, and the art does not teach, the genus broadly encompassed by the claims.

The specification discloses that the genus is inclusive of agents that include peptides, peptide mimetics, peptide-like molecules, mutant proteins, cDNAs, antisense oligonucleotides or constructs, lipids, carbohydrates, and synthetic or natural chemical

compounds (see paragraph 31, in particular). The genus is further inclusive of anything imaginable that blocks suppression of JNK activation by Gadd45β. However, the written description only reasonably conveys HIV-TAT-Peptide 1 fusion as an example of an agent that blocks suppression of JNK activation by Gadd45β.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Further, in regards to use of a product defined by function, without a correlation between structure and function, the claim does little more than define the product's function. That is not sufficient to satisfy the written description requirement. See Eli Lilly, 119 at1568 USPQ2d at 1406 ("definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of agents that encompass the genus nor does it provide a description of structural features that are common to the genus. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of HIV-TAT-Peptide 1 fusion is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, even though Applicant proposes methods of screening for possible members of the genus (paragraph 33, in particular), the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the

method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Further, due to the lack of a written description of which known pro-apoptotic factors function by blocking suppression of JNK activation by Gadd45β, it is unclear whether the claimed invention is inherently taught in the art.

In the Reply of 8/15/07, Applicant amended the claims and argues that limiting the claims to HIV-TAT-Peptide 1 fusion is unduly restrictive and gives no credence to the inventor's overall invention. Applicant further argues that the claims should not be limited to the HIV-TAT-Peptide 1 fusion because the inventors have demonstrated for the first time that preventing Gadd45β-JNKK2 interaction or binding results in increased cell death. Applicant further cites case law and states that (1) claims need not be limited to the preferred embodiment when the invention is more broadly described and (2) the court has cautioned against limiting the claimed invention to preferred embodiments or specific examples in the specification.

The amendments to the claims and the arguments found in the Reply of 8/15/07 have been carefully considered, but are not deemed persuasive. In regards to the argument that limiting the claims to HIV-TAT-Peptide 1 fusion is unduly restrictive and gives no credence to the inventor's overall invention, this rejection is based on whether a genus of products to be used in the invention is adequately described. While the specification teaches a single species of the genus, the HIV-TAT-Peptide 1 fusion, the specification does not adequately describe the genus of agents that block suppression of JNK activation by Gadd45β for the reasons discussed above. Without a description of said genus, one of skill in the art would not know what products would or would not function as agents that block suppression of JNK activation by Gadd45β and that could be selected to perform the claimed invention.

Further, in regards to the argument that the claims should not be limited to the HIV-TAT-Peptide 1 fusion because the inventors have demonstrated for the first time that preventing Gadd45β-JNKK2 interaction or binding results in increased cell death, whether or not inventors have demonstrated for the first time that preventing Gadd45β-JNKK2 interaction or binding results in increased cell death is not a basis for this rejection.

Further, in regards to the statement that claims need not be limited to the preferred embodiment when the invention is more broadly described, the genus of agents that block suppression of JNK activation by Gadd45β is not broadly described.

Further, in regards to the statement that the court has cautioned against limiting the claimed invention to preferred embodiments or specific examples in the

specification, the genus of agents that block suppression of JNK activation by Gadd45β is not adequately described for the reasons discussed above.

Claims 1, 6, and 36 remain rejected under 35 U.S.C. 112 first paragraph, for failing to comply with the enablement requirement, for the reasons stated in the Office Actions of 3/30/06, 11/29/06, and for the reasons set-forth below.

While being enabling for an *in vitro* method for increasing JNK activation leading to programmed cell death comprising selecting an agent comprising a cell-permeable peptide comprising amino acids 132-156 of SEQ ID NO:50 wherein said peptide blocks suppression of JNK activation by Gadd45β and treating cultured cells with said agent to increase programmed cell death of said cultured cells, does not reasonably provide enablement for *in vivo* methods for increasing JNK activation leading to programmed cell death comprising selecting an agent that blocks suppression of JNK activation by Gadd45β and using said agent to increase programmed cell death.

In the Reply of 8/15/07, Applicant argues that the law does not require that every conceivable embodiment to be tested and validated. Applicant further argues that none of the pending claims mention any particular disease in the preamble. Applicant further argues: "Although the examiner acknowledges that the PTO is not the FDA, the examiner uses the requirements of §112 as an option to impose FDA requirements for disease testing". Applicant further argues that a previous Office Action had not given due consideration or any deference to Gadd45β knock-out data. Applicant further argues that the in vitro models are standard and have been shown to reasonably

correlate to in vivo effects. Applicant concludes that showing that Gadd45β binds to and inhibits JNKK2 in vitro, thereby removing a barrier to apoptosis, coupled with evidence that absence of Gadd45β in vivo removes a barrier to apoptosis, is sufficient to support the pending claims.

The amendments to the claims and the arguments found in the Reply of 8/15/07 have been carefully considered, but are not deemed persuasive. In regards to the argument that the law does not require that every conceivable embodiment to be tested and validated, an enabling disclosure is not provided for *any* embodiment of an *in vivo* methods for increasing JNK activation leading to programmed cell death comprising selecting an agent that blocks suppression of JNK activation by Gadd45β and using said agent to increase programmed cell death.

Further, in regards to the argument that none of the pending claims mention any particular disease in the preamble, the broadly-drawn claims encompass methods of treating every disease to which an increase in cell death would be therapeutic. As disclosed in the specification, diseases to which an increase in cell death would be therapeutic include just any cancer (see paragraph 20, in particular). Clearly, the specification contemplates the claimed method as a method of treating cancer. Undue experimentation required for such in vivo treatment is addressed in the Office Action of 3/30/06.

Further, in regards to the argument that the examiner uses the requirements of §112 as an option to impose FDA requirements for disease testing, the examiner is making no attempts to impose FDA requirements for disease testing. Rather, this

rejection is based on factors to be considered in determining whether undue experimentation is required, as summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). Based on these factors, as discussed in the Office Actions of 3/30/06 and 11/29/06, it has been determined that it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

Further, in regards to the argument that the Office has not given due consideration or any deference to Gadd45β knock-out data, the Office Action of 11/29/06 contains the following text: "Applicant's arguments that the Franzoso Declaration data using Gadd45β knock-out mice and showing that JNK activation leads to cell death in mice following hepatectomy demonstrates that Gadd45β modulation of JNK pathway extends to in vivo models are not found to be persuasive because data is not commensurate in scope with the claimed invention for the following reasons: (i) the data does not show the treatment of any disease, as is contemplated by the

specification and is encompassed by the broadly drawn claims, and (ii) the data does not show the use of an agent that interacts with Gadd45β is effective in vivo, but rather shows physiological effects of complete Gadd45β gene knock-out. Thus, in view of the teaching set forth in the specification and further considering the data provided in the Franzoso declaration, one of skill in the art would not predict that the invention would function as claimed in vivo in the treatment of any disease, for example cancer, for the reasons set forth in the previous Office Action."

In regards to the argument that the in vitro models are standard and have been shown to reasonably correlate to in vivo effects, the unpredictability of how a method will function in vivo based on how said method functions in vitro is discussed in great depth in the Office Action of 3/30/06 (see pages 7-10 of the Office Action of 3/30/06, in particular).

For the reasons stated in the Office Actions of 3/30/06, 11/29/06, and for the reasons discussed above, a showing that Gadd45β binds to and inhibits JNKK2 in vitro, coupled with evidence that absence of Gadd45β in vivo removes a barrier to apoptosis, is not sufficient to support the pending broadly-drawn claims.

Double Patenting

Claims 1 and 6 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, and 6 of copending Application No. 10/263330 for the reasons stated in the Office Action of 8/30/06.

In the Reply of 8/15/07, Applicant states that a terminal disclaimer over U.S. Serial No. 10/263,330, if necessary, will be filed if the pending claims are allowable.

Summary

No claim is allowed. Again, due to the lack of a written description of the claimed invention, it is unclear whether the claimed invention is inherently taught in the art. Essentially, it is unclear whether known pro-apoptotic factors function by blocking suppression of JNK activation by Gadd45β.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA